The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 46

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte PAUL R. SCHIMMEL

Appeal No. 1997-2396[1]
Application No. 08/249,689[2]

HEARD: February 6, 2001

Before WILLIAM F. SMITH, SCHEINER and MILLS, Administrative Patent Judges.

SCHEINER, Administrative Patent Judge.

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[1] As a preliminary matter, we note that this appeal is related to an appeal in application serial no. 07/929,834 (Appeal No. 1997-3242). We have considered the two appeals together.

[2] Application for patent filed May 26, 1994. According to appellant, this application is a continuation of application serial no. 08/129,787, filed September 29, 1993, now abandoned, which is a continuation of application serial no. 07/586,534, filed September 21, 1990, now abandoned.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 and 3 through 21, all the claims remaining in the application.

REPRESENTATIVE CLAIMS

Claims 1, 11 and 21 are representative and read as follows:

1. A method for designing a compound specifically inhibiting targeted ribonucleic acid function comprising the steps of:

(a) determining the nucleotide sequence in the targeted ribonucleic acid that is critical to function;

(b) determining the secondary structure of the region of the targeted ribonucleic acid in which the critical site is located;

(c) determining the three-dimensional structure of the targeted RNA, including the position of the critical site relative to the major and minor grooves;

(d) determining the sequence of nucleotides and structure flanking the critical site in the targeted ribonucleic acid that is specific to the critical region of the ribonucleic acid to be inhibited and within the minor groove; and

(e) synthesizing a compound that will bind specifically to the critical site within the minor groove of the targeted ribonucleic acid thereby inhibiting targeted ribonucleic acid function.

11. A compound specifically binding to and inhibiting the function of a targeted RNA molecule, wherein the compound is specifically directed to and binds to a critical region of the RNA molecule, located withing the minor groove of the RNA molecule, identified by a combination of the primary, secondary and tertiary structure of the critical region.

21. The compound of claim 11 wherein the compound is a nucleic acid and the compound is synthesized in vivo from a retroviral vector.

ISSUES

Claims 1 and 3 through 21 stand rejected under 35 U.S.C. § 112, first paragraph, as not supported by an enabling disclosure. In addition, claims 11, 12 and 17 through 19 stand provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as copending application 07/929,834; and claims 1, 3 through 6, 8 through 10, 13 through 16, 20 and 21 stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as unpatentable over the claims of 07/929,834.

We reverse the enablement rejection, but affirm both provisional double patenting rejections. In addition, we enter a new ground of rejection under the provisions of 37 CFR § 1.196(b).

BACKGROUND

According to the specification, the invention "pertains generally to compounds and to the design of these compounds targeted to bind to ribonucleic acid [(RNA)]; and more particularly, to compounds that bind specifically to certain nucleotide base pairs in combination with elements of the secondary structure of the minor groove of [RNA] molecules." Page 1. Further according to the specification (pages 1 and 2):

> Three principal types of RNA exist in cells: messenger RNA, transfer RNA and ribosomal RNA. . . .
>
> The RNAs share a common overall structure, though each kind of RNA has a unique detailed substructure. Generally RNA is a linear, single-stranded . . . , repetitive polymer in which nucleotide subunits are covalently linked to each other in sequence. Each nucleotide subunit

> consists of a base linked to the ribose-phosphate of the polymeric backbone. The bases in RNA are adenine (A), uracil (U), guanine (G), and cytosine (C). The sequence of bases imparts specific function to each RNA molecule. Nucleotide bases from different parts of the same or different RNA molecules recognize and noncovalently bond with each other to form base pairs. Since RNAs generally are a single covalent strand, base pairing interactions are usually intrastranded . . . [and] play a major part in determining the three-dimensional structure of each of the RNAs and the interaction of RNA molecules with each other and with other molecules. . . .
>
> The RNA molecule forms a helix with major and minor grooves spiraling around the axis . . . Nucleotide bases are arranged near the center of the helix with the ribose phosphate backbone on the outside. The bases are planar, perpendicular to the axis, and stacked on one another. Because the helix is in the alpha form, bases and sequences of bases are most accessible from the minor groove, which is wider and more shallow than the major groove . . .

For a number of reasons discussed at length in the specification (e.g., pages 3, 4, 7, 8 and 17), "the primary basis for sequence discrimination in RNA is believed to be the minor groove." Specification, page 20. It is against this background that we consider the issues raised by this appeal.

DISCUSSION

Enablement

"The first paragraph of 35 U.S.C. § 112 requires, inter alia, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without 'undue experimentation.' In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir.

1988). That some experimentation may be required is not fatal; the issue is whether the amount of experimentation required is 'undue.'" In re Vaeck, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991) (emphasis in original).

A number of factors are relevant to whether undue experimentation would be required to practice the claimed invention, including "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The claimed invention is directed to compounds and methods of designing compounds that will bind to a critical site within the minor groove of a ribonucleic acid molecule and inhibit its function. The method comprises five fundamental steps: (a) identifying a nucleotide sequence (i.e., the primary structure) in an RNA molecule that is critical to its function; (b) determining the secondary structure of the region where the critical site is located; (c) determining the tertiary structure of the region where the critical site is located, and its position relative to the major and minor grooves of the molecule; (d) determining the sequence of nucleotides and structure flanking the critical site that is specific to the critical region and within the minor groove; and (e) synthesizing a compound that will specifically bind the critical site within the minor groove and inhibit RNA function. See, e.g., claims 1 and 11.

Following an analysis of each of the five steps under the Wands factors, the examiner concludes that it would have required undue experimentation to practice the claimed invention, and therefore, the claimed invention is not supported by an enabling disclosure. According to the examiner, one skilled in the art, after first turning to the specification, and then to the prior art for examples or other guidance, "would have been forced to turn to trial and error experimentation in an . . . unpredictable [art]." Examiner's Answer, page 11.

It may well be, as the examiner argues, that "[i]t is not predictable which nucleotides [will turn out to be] critical for function of an RNA molecule." Examiner's Answer, page 9. It may also be that "it is not predictable that [] critical sites exist [in the minor grooves of] all RNA molecules . . . [or] that the secondary and tertiary structures of all RNA molecules could be determined." Id., page 6. Nevertheless, we note the assertion in the specification that "RNA synthesis has developed sufficiently that it can now make available large amounts of otherwise scarce RNA species, such that structural analysis of these molecules is now feasible." Specification, page 36. In view of this, we agree with appellant that what matters here is that "the procedure[s] for determining which sites are critical can be performed as described in the specification with predictable results (i.e. the location of critical sites will be determined)," for at least

some RNA molecules.[3] Brief, page 20. Having carefully considered the respective positions of appellant (at pages 7 through 12 of the Brief) and the examiner (at pages 5 through 11 of the Examiner's Answer), we agree with appellant that, at least for steps (a) through (d), "the claimed method is a combination of procedures known in the art" and/or "described in the specification." Brief, page 12.

In reviewing the specification as a whole, it appears that appellant's focus on critical sites within the minor groove of an RNA molecule, where the nucleotide bases and their primary sequence are most accessible, takes the claimed invention out of the realm of trial and error experimentation. In our view, the only remaining question is this: having identified both the sequence and the local three-dimensional structure of a critical site within the minor groove of a target RNA molecule by performing steps (a)

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[3] To the extent that the examiner may be concerned that the method encompasses inoperative embodiments (i.e., RNA molecules with no critical sites located in minor grooves; RNA molecules with indeterminate structures), there is no evidence of record which would indicate that the claims encompass a significant number of inoperative embodiments. As set forth in Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., 750 F.2d 1569, 1576-77, 224 USPQ 409, 414 (Fed. Cir. 1984):

> Even if some of the claimed combinations were inoperative, the claims are not necessarily invalid. "It is not a function of the claims to specifically exclude . . . possible inoperative substances . . . . In re Dinh-Nguyen, 492 F.2d 856, 859-60, 181 USPQ 46, 48 (CCPA 1974) (emphasis omitted). Accord, In re Geerdes, 491 F.2d 1260, 1265, 180 USPQ 789, 793 (CCPA 1974); In re Anderson, 471 F.2d 1237, 1242, 176 USPQ 331, 334-35 (CCPA 1971). Of course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid. See, e.g., In re Cook, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971).

through (d) of the claimed method, would it have required undue experimentation for one skilled in the art to design a compound that would specifically bind the critical site and inhibit RNA function?

With respect to this last step of the claimed method, the examiner concedes that "[t]he specification provides general guidance . . . to use known computer modeling programs to test hypothetical structures . . . for interaction with a substrate of known structure," but argues that it "does not provide specific guidance" or "a working example of designing a compound that specifically interacts with a critical site comprising a minor groove on an RNA molecule resulting in [inhibition of RNA function];" and "[i]t is unpredictable whether computer-aided design can be used" to do so. Examiner's Answer, pages 6 through 8 and 10. Finally, the examiner relies on Wilson[4] as evidence that, even three years after the filing date, the art "did not show the claimed invention." Examiner's Answer, page 18.

On the other hand, according to the specification, at the time of the invention, various computer modeling systems had been used to resolve the three-dimensional structures of specific proteins, and also to design molecules specifically interactive with them. Further according to the specification, compounds having specific interactions with nucleic acids were known, and a great deal was known about the structural basis

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[4] Wilson et al (Wilson), "The Search for Structure-Specific Nucleic Acid-Interactive Drugs: Effects of Compound Structure on RNA versus DNA Interaction Strength," Biochemistry, Vol. 32, pp. 4098-4104 (1993).

of those interactions. Pages 37 through 39. Finally, as discussed above, the specification indicates that contemporaneous advances in RNA synthesis had made previously scarce RNA molecules available for structural analysis by computer modeling. Id., page 36. Once the sequence and local three-dimensional structure of a critical site in a targeted RNA molecule are elucidated by computer modeling, the specification teaches that "[s]pecific binding to the targeted molecule can be achieved by including in the molecule [a] complementary nucleic acid sequence that forms base pairs with the targeted RNA . . . or by inclusion of chemical groups having the correct spatial location and charge." Id., page 38.

It is well settled that the examiner bears the initial burden of providing reasons why a supporting disclosure does not enable a claim. As stated in In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971):

> [A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

While the factors relied on by the examiner are relevant in determining whether the claimed invention is enabled by the specification, we hold that, on balance, they are insufficient to establish a reasonable basis to doubt the objective truth of statements regarding design and synthesis of compounds to bind and inhibit the function of RNA molecules. Accordingly, we hold that the examiner has not established that the

experimentation required to practice the claimed invention would be undue. The examiner's rejection of claims 1 and 3 through 21 for lack of enablement under 35 U.S.C. § 112, first paragraph, is reversed.

Double Patenting

Claims 11, 12 and 17 through 19 stand provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 15 through 19 of copending application 07/929,834. Claims 1, 3 through 6, 8 through 10, 13 through 16, 20 and 21 stand provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as unpatentable over claims 1 through 5, 8 through 10, 12 through 14 and 22 of 07/929,834. Appellant does not dispute the merits of either rejection. See the Reply Brief, page 2. As appellant has not argued that the rejections are improper, we affirm them both.

NEW GROUND OF REJECTION

Written Description

Under the provisions of 37 CFR § 1.196(b), we make the following new ground of rejection: Claims 11 through 13, 17 through 19 and 21 are rejected under the first paragraph of 35 U.S.C. § 112 because the specification fails to provide an adequate written description of the claimed invention.

The Federal Circuit has recently clarified the application of the written description requirement of the first paragraph of § 112 to inventions in the field of

biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court explained that

> In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus . . . [H]owever, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. The court also stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. at 1567, 43 USPQ2d at 1405. Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id. at 1568, 43 USPQ2d at 1406.

Claim 21 is directed to nucleic acid compounds defined only by their ability to bind within the minor groove of an unspecified RNA molecule and inhibit its function. In other words, the claimed compounds are defined in functional, rather than structural terms. Claims 11 through 13 and 17 through 19 are even broader than claim 23, in that they are not limited to nucleic acids. For example, the compound of claim 11 is described simply as "specifically binding to and inhibiting the function of a targeted RNA molecule, wherein the compound is specifically directed to and binds to a critical region of the RNA molecule, located within the minor groove of the RNA molecule."

The specification does not identify or describe a single compound meeting the limitations of the claims, nor does it describe structural features common to the members of the claimed genus which would constitute a substantial portion of the genus. In the absence of a precise definition of a representative number of the claimed compounds, such as by structure, formula, or chemical name, one skilled in the art could not envision the members of the genus recited in even the narrowest claim (claim 21). We therefore conclude that the claimed compounds are not adequately described. Accordingly, claims 11 through 13, 17 through 19 and 21 are rejected under 35 U.S.C. § 112, first paragraph, because they are not supported by an adequate written description of the claimed invention.

OTHER MATTERS

Today we introduce a new ground of rejection under the "written description" provision of the first paragraph of 35 U.S.C. § 112, while reversing the examiner's

rejection of the same claims under the "enablement" ("make and use") provision of the statute. While these actions might appear to be inconsistent at first glance, the severability of the two provisions has long been recognized. See Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1561, 19 USPQ2d 1111, 1115. As explained in Vas-Cath,

> In a 1971 case [] involving chemical subject matter, the [Court of Customs and Patent Appeals] expressly stated that "it is possible for a specification to enable the practice of an invention as broadly as it is claimed, and still not describe that invention." In re DiLeone, 436 F.2d 1404, 1405, 168 USPQ 592, 593 (CCPA 1971) (emphasis added). As an example, the court posited the situation "where the specification discusses only compound A and contains no broadening language of any kind. This might very well enable one skilled in the art to make and use compounds B and C; yet the class consisting of A, B and C has not been described. Id. at 1405 n. 1, 168 USPQ 593 n. 1 (emphases in original).

Id. at 1561-62, 19 USPQ2d at 1115.

Upon application of the relevant standards, we conclude that there is no inconsistency in our determination that appellant's specification would have enabled one skilled in the art to make and use compounds with the required functional properties, but nevertheless fails to describe such compounds.

CONCLUSION

We have reversed the rejection of claims 1 and 3 through 21 for lack of enablement, but affirmed the provisional double patenting rejections of claims 1, 3 through 6, and 8 through 21. In addition, we enter a new ground of rejection of claims 11 through 13, 17 through 19 and 21 under the provisions of 37 CFR § 1.196(b). As a result of our action today, claim 7 is free of rejection.

TIME PERIOD FOR RESPONSE

In addition to affirming the examiner's rejection of one or more claims, this decision contains a new ground of rejection pursuant to 37 CFR § 1.196(b) (amended effective Dec. 1, 1997, by final rule notice, 62 Fed. Reg. 53, 131, 53, 197 (Oct. 10, 1997), 1203 Off. Gaz. Pat & Trademark Office 63, 122 (Oct. 21, 1997)). 37 CFR § 1.196(b) provides, "A new ground of rejection shall not be considered final for purposes of judicial review."

> Regarding any affirmed rejection, 37 CFR § 1.196(b) provides:
> (b) Appellants may file a single request for rehearing within two months from the date of the original decision . . .

37 CFR § 1.196(b) also provides that the appellant, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of proceedings (37 CFR § 1.197(c)) as to the rejected claims:

> (1) Submit an appropriate amendment of the claims so rejected or a showing of facts related to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the application will be remanded to the examiner . . . .
>
> (2) Request that the application be reheard under 37 CFR § 1.197(b) by the Board of Patent Appeals and Interferences upon the same record . . . .

Should appellant elect to prosecute further before the Primary Examiner pursuant to 37 CFR § 1.196(b)(1), in order to preserve the right to seek review under 35 U.S.C. §§ 141 or 145 with respect to the affirmed rejection, the effective date of the

affirmance is deferred until conclusion of the prosecution before the examiner unless, as a mere incident to the limited prosecution, the affirmed rejection is overcome.

If appellant elects prosecution before the examiner and this does not result in allowance of the application, abandonment or a second appeal, this case should be returned to the Board of Patent Appeals and Interferences for final action on the affirmed rejection, including any timely request for rehearing thereof.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN PART; 1.196(b)

William F. Smith
Administrative Patent Judge

Toni R. Scheiner
Administrative Patent Judge

Demetra J. Mills
Administrative Patent Judge

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) APPEALS AND
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Appeal No. 1997-2396
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